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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/759,372	01/15/2004	Liyan He	559812000100	9939

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EXAMINER	
POHNERT, STEVEN C	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 11/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/759,372	HE, LIYAN	
	Examiner	Art Unit	
	Steven C. Pohnert	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) *26-30 and 52-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25 and 31-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date ~~8/10/2005~~. 9/17/2004 SP
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of group 1, claims 1-25 and 31 -51 in the reply filed on 8/17/2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 26-30 and 52-58 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim.

A first action on the merits of claims 1-25 and 31-51 follows.

Specification

2. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-5, 7-16, 18, 20-24, 31-44, 46-50 are rejected under 35 U.S.C. 102(b) as being anticipated by Lizardi et al (US Patent 6261782).

With regards to claim 1, Lizardi et al teaches treating DNA with a type IIs endonuclease (see column 25, line 27-31). Lizardi further teaches ligation of adapters with all possible combination of nucleic acid sequences (see column 25, lines 35-65). Lizardi teaches the blocking of adapters so as to inhibit ligation (see column 29, lines 34-36). Lizardi further teaches ligation of adapters to DNAs (see column 29, lines 60-61). Lizardi further teaches generation of circularized DNA by ligation (see column 28, lines 65-67). Lizardi thus teaches ligating adapters that are blocked into a plasmid resulting in circular DNA with a continuous and discontinuous strand.

With regards to claim 2-5, Lizardi teaches use of FokI, a type IIS endonuclease, which results in a 4 nucleotide protrusion (see column 25, lines 25-33).

With regards to claim 7, Lizardi teaches the blocking of adapters so as to inhibit ligation (see column 29, lines 34-36).

With regards to claims 8 and 9, Lizardi teaches the adapter has a biotin capture tag that can be used to bind a partner on a solid support (see column 20, line 16-19).

With regards to claim 10, Lizardi teaches binding of biotin labeled adapters to immobilized avidin (see column 51, lines 26-28), washing to remove unbound fragments, denaturing DNA with NaOH, and releasing the complementary non-bound strand (see column 63, lines 7-10). This is interpreted as immobilizing circular indexed, washing, denaturing and collecting circular indexed fragments.

With regards to claim 11, Lizardi teaches the use of glass, polystyrene, Teflon, nylon as substrates (see column 20, lines 38-42).

With regards to claim 12, Lizardi et al teaches treating DNA with a type IIs endonuclease (see column 25, line 27-31). Lizardi further teaches ligation of adapters with all possible combination of nucleic acid sequences (see column 25, lines 35-65). Lizardi teaches the blocking of adapters so as to inhibit ligation (see column 29, lines 34-36). Lizardi further teaches ligation of adapters to DNAs (see column 29, lines 60-61). Lizardi further teaches generation of circularized DNA by ligation (see column 28, lines 65-67). Lizardi thus teaches ligating adapters that are blocked into a plasmid resulting in circular DNA with a continuous and discontinuous strand. Thus Lizardi teaches generation of continuous and discontinuous circular DNA by ligation and rolling circle amplification.

With regards to claim 13-16, Lizardi teaches use of FokI, a type IIs restriction endonuclease, which results in a 4 nucleotide protrusion (see column 25, lines 25-33).

With regards to claim 18, Lizardi teaches the blocking of adapters so as to inhibit ligation (see column 29, lines 34-36).

With regards to claim 20-21 Lizardi teaches the adapter has a biotin capture tag that can be used to bind a partner on a solid support (see column 20, line 16-19).

With regards to claim 22, Lizardi teaches immobilized samples are amplified by suitable amplification (see column 57, lines 57-58), including rolling circle amplification (see Column 58, lines 37-39).

With regards to claim 23, Lizardi teaches the use of glass, polystyrene, teflon, nylon as substrates (see column 20, lines 38-42).

With regards to claim 24, Lizardi teaches immobilized index sample are amplified by suitable amplification methods (see column 57, lines 57-59). Lizardi teaches rolling circle amplification is a suitable amplification method (see column 58, lines 35-39). Thus Lizardi teaches rolling circle amplification on a surface.

With regards to claim 31, Lizardi et al teaches treating DNA with a type IIs endonuclease (see column 25, line 27-31). Lizardi further teaches ligation of adapters with all possible combination of nucleic acid sequences (see column 25, lines 35-65). Lizardi teaches the blocking of adapters so as to inhibit ligation (see column 29, lines 34-36). Lizardi further teaches ligation of adapters to DNAs (see column 29, lines 60-61). Lizardi further teaches generation of circularized DNA by ligation (see column 28, lines 65-67). Lizardi thus teaches ligating adapters that are blocked into a plasmid resulting in circular DNA with a continuous and discontinuous strand. Thus Lizardi teaches generation of continuous and discontinuous circular DNA by ligation and rolling circle amplification.

With regards to claim 32, Lizardi teaches an adapter can include producing end opposite the sticky end (see column 12 lines 38-41) and that they have the same length (see column 12, lines 5-8).

With regards to claim 33, Lizardi et al teaches the use of restriction endonucleases AciI and FokI. AciI results in a 2 base protrusion and FokI results in a 4 base protrusion. Lizardi thus teaches a method where the 5' and 3' protruding strands are different lengths.

With regards to claim 34, Lizardi teaches the use of FokI to cleave DNA. This results in overhangs of 4 nucleotides.

With regards to claim 35, Lizardi teaches the blocking of adapters so as to inhibit ligation (see column 29, lines 34-36).

With regards to claim 36-37, Lizardi teaches the adapter has a biotin capture tag that can be used to bind a partner on a solid support (see column 12, line 26-27).

With regards to claim 38, Lizardi teaches denaturing DNA with NaOH, and releasing the complementary non-bound strand (see column 63, lines 7-10).

With regards to claim 39, Lizardi et al teaches treating cDNAs with a type IIs endonuclease (see column 50, line 24) (a). Lizardi further teaches ligation of adapters with all possible combination of nucleic acid sequences (see column 50, lines 28-32)(b). Lizardi teaches the blocking of adapters so as to inhibit ligation (see column 29, lines 34-36). Lizardi further teaches ligation of adapters to cDNAs (see column 50, lines 51-60)(c). Lizardi further teaches generation of circularized DNA by ligation (see column 52, lines 48-52). Lizardi further teaches amplifying by rolling circle amplification (see column 52, lines 45-48). Thus Lizardi teaches generation of continuous and discontinuous circular DNA by ligation and rolling circle amplification.

With regards to claim 40, Lizardi teaches adapter can include producing end opposite the sticky end (see column 12 lines 38-41) and that they have the same length (see column 12, lines 5-8).

With regards to claim 41, Lizardi et al teaches the use of restriction endonucleases AciI and FokI. AciI results in a 2 base protrusion and FokI results in a 4

base protrusion. Lizardi thus teaches a method where the 5' and 3' protruding strands are different lengths.

With regards to claim 42, Lizardi teaches the use of FokI to cleave DNA. This results in overhangs of 4 nucleotides.

With regards to claim 43, Lizardi teaches the blocking of adapters so as to inhibit ligation (see column 29, lines 34-36).

With regards to claim 44, Lizardi teaches denaturing DNA with NaOH, and releasing the complementary non-bound strand (see column 63, lines 7-10).

With regards to claims 46 and 47, Lizardi teaches the adapter has a biotin capture tag that can be used to bind a partner on a solid support (see column 12, line 26-27).

With regards to claim 48 and 50, Lizardi teaches immobilized samples are amplified by suitable amplification (see column 57, lines 57-58), including rolling circle amplification (see Column 58, lines 37-39). Thus Lizardi teaches rolling circle amplification of a solid surface.

With regards to claim 49, Lizardi teaches the use of glass, polystyrene, teflon, nylon as substrates (see column 20, lines 38-42).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 6 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lizardi et al (US Patent 6261782) in view of Deugau et al (US Patent 5508169).

Lizardi et al teaches treating cDNAs with a type IIs endonuclease (see column 50, line 24) (a). Lizardi further teaches ligation of adapters with all possible combination of nucleic acid sequences (see column 50, lines 28-32)(b). Lizardi teaches the blocking of adapters so as to inhibit ligation (see column 29, lines 34-36). Lizardi further teaches ligation of adapters to cDNAs (see column 50, lines 51-60)(c). Lizardi further teaches generation of circularized DNA by ligation (see column 52, lines 48-52). Lizardi further teaches amplifying by rolling circle amplification (see column 52, lines 45-48).

Lizardi does not teach the use of interrupted palindrome endonucleases (claims 6 and 17).

However, Deugau teaches the use of interrupted palindrome endonucleases. Deugau teaches interrupted palindrome endonucleases like type IIs restriction endonucleases produce permutations and combinations of nucleotides on sticky ends suitable for indexing (see column 7, lines 42-48).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use interrupted palindrome endonucleases as the restriction enzymes in Lizardi's method of indexing and rolling circle amplification. The ordinary artisan would be motivated to use interrupted palindrome endonucleases as the restriction enzyme for indexing because Deugau teaches interrupted palindrome

endonucleases produce permutations and combinations of nucleotides on sticky ends suitable for indexing. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the instant invention was made, it must be considered that said ordinary skilled artisan would have had reasonable expectation of success in practicing the claimed invention.

7. Claims 19, 25, 45, and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lizardi et al (US Patent 6261782) in view of Lizardi (US Patent 6287824).

Lizardi et al '782 teaches treating cDNAs with a type IIs endonuclease (see column 50, line 24) (a). Lizardi '782 further teaches ligation of adapters with all possible combination of nucleic acid sequences (see column 50, lines 28-32)(b). Lizardi '782 teaches the blocking of adapters so as to inhibit ligation (see column 29, lines 34-36). Lizardi '782 further teaches ligation of adapters to cDNAs (see column 50, lines 51-60)(c). Lizardi '782 further teaches generation of circularized DNA by ligation (see column 52, lines 48-52). Lizardi '782 further teaches amplifying by rolling circle amplification (see column 52, lines 45-48). Lizardi '782 teaches the adapter has a biotin capture tag that can be used to bind a partner on a solid support (see column 12, line 26-27). Lizardi '782 teaches immobilized samples are amplified by suitable amplification (see column 57, lines 57-58), including rolling circle amplification (see Column 58, lines 37-39). Lizardi '782 teaches the use of glass, polystyrene, teflon, nylon as solid supports upon which rolling circle amplification can be done (see column 20, lines 38-42).

Lizardi '782 does not teach the use of a discontinuous strand as a primer for rolling circle amplification (claims 19 and 45) or separation of discontinuous strands before rolling circle amplification (claims 25 and 51).

However Lizardi '824 teaches the use of the discontinuous strand as a primer (se column 20, lines 32-33) (claim 19 and 45). Lizardi '824also teaches separation of the discontinuous strand before rolling circle amplification (see column 24, lines 38-42). Lizardi '824 teaches separation of the discontinuous strand allows more efficient rolling circle replication (see column 24, lines 39-40).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to incorporate the use of the secondary strand as a primer for RCA or separation of the second strand before RCA as taught by Lizardi '824 with the indexing and rolling circle amplification of Lizardi '782. The ordinary artisan would be motivated to use the secondary strand as a primer to obviate the need to add another primer and minimize steps required be eliminating the strand separation step. The ordinary artisan would be motivated to separate strands before rolling circle amplification because Lizardi '824 teaches separation improves efficiency of rolling circle replication. Given the teachings of the prior art and the level of skill of the ordinary skilled artisan at the time the instant invention was made, it must be considered that said ordinary skilled artisan would have had reasonable expectation of success in practicing the claimed invention.

No claims are allowed over prior art cited.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven C. Pohnert whose telephone number is 571-272-3803. The examiner can normally be reached on Monday-Friday 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Steven Pohnert

JEHANNE SITTON
PRIMARY EXAMINER
11/8/06